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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/088,966	03/22/2002	Reiner Grabowski	216180	4911

23460 7590 05/16/2005

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EXAMINER	
CALAMITA, HEATHER	

ART UNIT	PAPER NUMBER
1637	

DATE MAILED: 05/16/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/088,966	GRABOWSKI ET AL.	
	Examiner	Art Unit	
	Heather G. Calamita, Ph.D.	1637	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *24 March 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *75-95* is/are pending in the application.

4a) Of the above claim(s) *75-85* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *86-95* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *22 March 2002* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date 3/22/02
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

1. Applicant's election with traverse of Group II, claims 86-95 and SEQ ID NOs 2 and 25 filed on March 24, 2005 is acknowledged. Applicant's arguments filed 03/24/2005 have been fully considered but they are not persuasive. Traversal was on the grounds the subject matter of claims 75-95 is interrelated to the extent that a search and examination of the groups together would not be overburdensome. The examiner maintains that the search and examination of the groups together would be burdensome for the reasons stated in the office action mailed on February 22, 2005. Additionally, applicants assert that MPEP 803.04 allows for up to 10 independent sequences to be examined in an application. The examiner submits 2 sequences are within the parameter of up to 10. Applicant further discusses homology of the independent sequences and the intended use of the sequences and as such searching the sequences together would not impose undue burden. While the sequences may be homologous, they are not identical and therefore would require separate searches on various databases, imposing a burden on the office. Further the search required for the products (claims 75-85) does not overlap with the search required for the method claims (86-95). The search for the method claims would involve a text search to look for various method steps which would not be required for the search of the product claims. The examiner maintains the restriction requirement made previously, as each group is correctly separated as unrelated or patentably distinct and the restriction is **herein made final.** Claims 75-85 are withdrawn from further consideration by the examiner, 37 CFR 1.14(b), as being drawn to a non-elected invention. Pending claims to be examined are claims 86-95 and SEQ ID NOs 2 and 25.

Claim Rejections - 35 USC § 112

2. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 86-95 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. It is vague and indefinite what is meant for the term "analogous." The specification does not define the term and it is not a term of art. Therefore the metes and bounds of the claim cannot be determined. As such two rejections will be made. The 102 will rely on a broad reading of "analogous" and the 103 will not rely on a broad interpretation.

Claim Rejections - 35 USC § 102

3. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 86-95 are rejected under 35 U.S.C. 102(b) as being anticipated by Mariani et al. (USPN 5,654,141, 08/05/1997).

With regard to claims 86-95, Mariani et al. do not teach a primer pair that is identical to SEQ ID NOs 2 and 25 as the primer pair, but teach a primer pair that is interpreted as analogous to the primer pair of SEQ ID NOs 2 and 25 (see col. 4 lines 33-35, 44-46 and 48-55).

With regard to claim 86, Mariani et al. teach a method for detecting bacteria in an analytical sample, comprising

the step of bringing the analytical sample into contact with a nucleic acid or a combination of nucleic acids, and detecting suitable hybrid nucleic acids comprising the added nucleic acid and bacterial nucleic acid (see col. 2 lines 10-16).

With regard to claims 87 and 91, Mariani et al. teach the bacteria are enterobacteria (see col. 2 lines 52 and 54 and example 1). E. coli are enterobacteria.

With regard to claims 88 and 93, Mariani et al. teach the process involves a PCR amplification of the nucleic acid to be detected (see col. 5 lines 40-44).

With regard to claims 89 and 94, Mariani et al. teach in that the process involves a Southern Blot hybridization (see col. 8 lines 8-9).

With regard to claim 90, Mariani et al. teach the step of bringing the analytical sample into contact with a nucleic acid or a combination of nucleic acids and detecting suitable hybrid nucleic acids comprising the added nucleic acid and bacterial nucleic acid (see col. 2 lines 10-16).

With regard to claim 92, Mariani et al. teach a method for amplifying bacterial DNA of a multiplicity of different taxonomic units, especially genera and species, using primers in which in a first amplification step the DNA for high taxonomic units such as classes, phyla or families is amplified with conserved primers (see col. 4 lines 21-29, and 38-43). The 16S rRNA gene is conserved, and the target nucleic acids are from the classes of Escherichia, Streptococcus, Staphylococcus and Bacteroides. And, optionally, in a further step, the DNA fragments obtained by amplification which are specific for genera or species are detected by means of probes (see col. 8 lines 39-56).

With regard to claim 95, Mariani et al. teach a method for amplifying bacterial DNA of a multiplicity of different taxonomic units, especially genera and species, using primers in which in a first amplification step the DNA for high taxonomic units such as classes, phyla or families is amplified with conserved primers (see col. 4 lines 21-29, and 38-43), and, optionally, in a further step, the DNA fragments obtained by amplification which are specific for genera or species are detected by means of probes (see col. 8 lines 39-56).

Claim Rejections - 35 USC § 103

4. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 86-95 are rejected under 35 U.S.C. 103(a) as being unpatentable over Mariani et al. (USPN 5,654,141, 08/05/1997) in view of Yamamoto et al. (Genebank Accession number AB001341, submitted January 25, 1997).

With regard to claim 86, Mariani et al. teach a method for detecting bacteria in an analytical sample, comprising

the step of bringing the analytical sample into contact with a nucleic acid or a combination of nucleic acids, and detecting suitable hybrid nucleic acids comprising the added nucleic acid and bacterial nucleic acid (see col. 2 lines 10-16).

With regard to claims 87 and 91, Mariani et al. teach the bacteria are enterobacteria (see col. 2 lines 52 and 54 and example 1). E. coli are enterobacteria.

With regard to claims 88 and 93, Mariani et al. teach the process involves a PCR amplification of the nucleic acid to be detected (see col. 5 lines 40-44).

With regard to claims 89 and 94, Mariani et al. teach in that the process involves a Southern Blot hybridization (see col. 8 lines 8-9).

With regard to claim 90, Mariani et al. teach the step of bringing the analytical sample into contact with a nucleic acid or a combination of nucleic acids and detecting suitable hybrid nucleic acids comprising the added nucleic acid and bacterial nucleic acid (see col. 2 lines 10-16).

With regard to claim 92, Mariani et al. teach a method for amplifying bacterial DNA of a multiplicity of different taxonomic units, especially genera and species, using primers in which in a first amplification step the DNA for high taxonomic units such as classes, phyla or families is amplified with conserved primers (see col. 4 lines 21-29, and 38-43). The 16S rRNA gene is conserved, and the target nucleic acids are from the classes of Escherichia, Streptococcus,

Staphylococcus and Bacteroides. And, optionally, in a further step, the DNA fragments obtained by amplification which are specific for genera or species are detected by means of probes (see col. 8 lines 39-56).

With regard to claim 95, Mariani et al. teach a method for amplifying bacterial DNA of a multiplicity of different taxonomic units, especially genera and species, using primers in which in a first amplification step the DNA for high taxonomic units such as classes, phyla or families is amplified with conserved primers (see col. 4 lines 21-29, and 38-43), and, optionally, in a further step, the DNA fragments obtained by amplification which are specific for genera or species are detected by means of probes (see col. 8 lines 39-56).

With regard to claims 86-95, Mariani et al. do not teach SEQ ID NOs 2 and 25 as the primer pair, using a narrow interpretation of the claim as per 112 2nd above.

Yamamoto et al. teach SEQ ID NOs 2 and 25 (see alignment below).

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Claimed SEQ ID NO: 2    1 ttcgggttgtcatgccaatg 20

Yamamoto et al.     11799 ttcgggttgtcatgccaatg 11780


Claimed SEQ ID NO: 25 1 ccgccaggcaaattctgt 18

Yamamoto et al.    11482 ccgccaggcaaattctgt 11499
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It would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to combine the method of Mariani with the use of functionally equivalent primers selected from the sequences of Yamamoto since Mariani expressly teaches primer selection using primers which amplify specific sequences in E. coli in order to detect the presence of the bacteria in patient samples.

In the recent court decision *In Re Deuel* 34 USPQ 2d 1210 (Fed. Cir. 1995), the Court of Appeals for the Federal Circuit determined that the existence of a general method of identifying a

specific DNA does not make the specific DNA obvious. Regarding structural or functional homologs, however, the Court stated,

"Normally, a *prima facie* case of obviousness is based upon structural similarity, i.e., an established structural relationship between a prior art compound and the claimed compound. Structural relationships may provide the requisite motivation or suggestion to modify known compounds to obtain new compounds. For example, a prior art compound may suggest its homologs because homologs often have similar properties and therefore chemists of ordinary skill would ordinarily contemplate making them to try to obtain compounds with improved properties (see page 9, paragraph 4 of attached ref)."

Since the claimed primers simply represent structural homologs, which are derived from sequences suggested by the prior art as useful for primers for the detection of E. coli and concerning which a microbiologist of ordinary skill would attempt to obtain alternate compounds with improved properties, the claimed primers are *prima facie* obvious over the cited references in the absence of secondary considerations.

Buck expressly provides evidence of the equivalence of primers. Specifically, Buck invited primer submissions from a number of labs (39) (page 532, column 3), with 69 different primers being submitted (see page 530, column 1). Buck also tested 95 primers spaced at 3 nucleotide intervals along the entire sequence at issue, thereby testing more than 1/3 of all possible 18 mer primers on the 300 base pair sequence (see page 530, column 1). When Buck tested each of the primers selected by the methods of the different labs, Buck found that EVERY SINGLE PRIMER worked (see page 533, column 1). Only one primer ever failed, No. 8, and that primer functioned when repeated. Further, EVERY SINGLE CONTROL PRIMER functioned as well (see page 533, column 1). Buck expressly states "The results of the empirical sequencing analysis were surprising in that nearly all of the primers yielded data of extremely high quality (page 535, column 2)." Therefore, Buck provides direct evidence that all primers would be expected to function, and in particular, all primers selected according to the ordinary criteria, however different, used by 39 different laboratories. It is particularly striking that all 95 control primers functioned, which represent 1/3 of all possible primers in the target region. This clearly shows that every primer would have a reasonable expectation of success.

Summary

5. No claims allowed.

Conclusion

6. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Heather G. Calamita whose telephone number is 571.272.2876 and whose e-mail address is heather.calamita@uspto.gov. However, the office cannot guarantee security through the e-mail system nor should official papers be transmitted through this route. The examiner can normally be reached on weekdays 7:00 A.M. - 5:30 P.M..

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Benzion can be reached on 571.272.0782. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

hgc

JEFFREY FREDMAN
PRIMARY EXAMINER
5/3/05